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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/645,556	08/25/2000	Bernward Scholkens	02481.1702	3278

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EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 11/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/645,556	SCHOLKENS ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,6 and 19-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,6 and 19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/18/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 13, 2005 has been entered.

Action Summary

The rejection of claims 4, 6 and 19 under 35 U.S.C. 103(a) as being unpatentable over Bussien et al. (Naunyn-Schmiedelberg's Archives of Pharmacology, 1985) of record in view of Simmons (U.S.Patent No. 5,656,603) is hereby expressly withdrawn.

Upon further consideration and in view of amendment, following new ground (s) of rejection has been made.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 4, 6 and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bussien et al. (Naunyn-Schmiedelberg's Archives of Pharmacology,

1985) of record in view of Physicians' Desk Reference (PDR), 1999 (published 1998, Dec. 14).

Bussien et al. teach ramipril (HOE 498) was evaluated in 12 normotensive male volunteers aged 21 to 26. Bussien et al. teaches ramipril was administered orally in a single dose of 2.5, 5, 10 or 20mg to groups of normal volunteers. (abstract). Bussien et al. suggests that the 5mg dose of HOE 498 expected to be adequate for the treatment of hypertension and congestive heart failure. (page 67 right hand column).

Bussien et al. do not teach the previous medical history of the normotensive male volunteers and the employment of ramiprilat for the method set forth in claim 4.

PDR teaches that ramipril is almost completely metabolized to Ramiprilat, which as about 6 times the ACE inhibitory activity of ramipril. (Page 1294, right-hand column lines 7-11). PDR teaches prescribing information of ramipril including description, mechanism of action, indications and usage, contraindications and adverse reaction. (page 1293-1295).

It would have been obvious to one of ordinary skill in the art to employ Ramipril or Ramiprilat for reducing the risk of onset of congestive heart failure regardless of their previous medical history because Bussien et al. teach that ramipril can be administered in normotensive patients and can also be employed for treating hypertension and congestive heart failure and because ramiprilat is the metabolite of ramipril that was about 6 times the ACE inhibitory activity of ramipril as taught by PDR. One would have been motivated to employ ramipril to normotensive patients regardless of their previous medical history to reduce the chance of having congestive heart failure in order to

successfully achieve the expected benefit of ramipril in adequate treatment of congestive heart failure because there is no warnings or contraindications or adverse reactions indicated by PDR that there is risk involved wit such medical history. Absent any evidence to contrary, there would have been a reasonable expectation of successfully reducing the risk of onset of congestive heart failure by administration of ramipril or ramiprilat which are effective for treating congestive heart failure as taught by Bussien et al. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

None of the claims are allowed.

Response to Arguments

Applicants arguments filed September 13, 2005 have been fully considered but they are not persuasive. Applicants argue that Bussien do not teach or suggest the administration of the ramipril or ramiprilat to the patient who has a history of previous ischaemic heart disease, stroke, or peripheral arterial disease or the patient has diabetes. This is not persuasive because the Examiner has made an obviousness rejection. It is the Examiner's position that Bussien teaches that the male volunteer are **normotensive (person with a normal blood pressure)** which encompasses Applicants' limitation of "who has an essentially maintained heart function and ... who exhibits normal blood pressure". Further, whether the volunteers has had a previous

medical **history** or not, is not a patentable limitation and the cited Bussan encompasses any current normotensive patients may also include their any other medical history.. Including the limitation of previously suffered from ischeaemic heart disease, stroke or peripheral arterial diseases or that they has had diabetes. Bussian et al teach any normotensive patients at present, regardless of the medical history and PDR does not indicate that there is a problem administering ramipril or ramiprilat to a patient with such medical history. Therefore, in this case, one of ordinary skill in the art would employ ramipril to normotensive patients as taught by Bussien et al. in order to reduce a chance of having congestive heart failure as suggested by Bussien et al. that ramipril is expected to treat congestive heart failure. Applicant's attention is drawn to Physician's Desk Reference, 1999 Edition, on page,1293-1296, under ALTACE® (ramipril), no where in this content indicates that ramipril is contraindicated or it is not suitable for the patients with a medical history of previous ischaemic heart disease, stroke, or peripheral arterial disease or the patient has diabetes. One of ordinary skill in the art would have been motivated to employ the ramipril regardless of their medical history of previous ischaemic heart disease, stroke, or peripheral arterial disease or the patient has diabetes because there is no proviso or provision or contraindication that ramipril can not be employed. Applicants argument that the cited articles, "Prevention Trial" and "Treatment Trial" of heart failure as part of the Studies of Left Ventricular Dysfunction with the ACE inhibitor enalapril, PEACE trial with the ACE inhibitor Trandolapril, SOLVD trial or SAVE trial involving captopril reflects how those skilled in the art would have interpreted the trials and how the results of those trials did not create an expectation of

success in performing the method of the invention in a patient population having an essentially maintained heart function and how direct evidence of efficacy in the new patient population was important. This is not persuasive the cited articles do not involve with the specific active agent at issue, ramipril or ramiprilat. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sreenivasan Padmanabhan
Supervisory Examiner
Art Unit 1617

Jmk
October 26, 2005